nerve action potential (SNAP) amplitude, and nerve conduction velocity (NCV)). These results were correlated with peroneus muscle and peroneal nerve histology.

Results: Baseline physiologic characteristics were similar between groups. Neuromuscular recovery in groups with early restoration of flow (Control, 1HR, 3HR) was similar and nearly complete (92%, 98% and 88% respectively; $p > 0.45$). While recovery was diminished in both 6HR and Ligation; Ligation, rather than repair, exhibited greater recovery (68% vs 53%; $p < 0.05$). These relationships correlated with the pathologic grade of degeneration, necrosis, and fibrosis ($p < 0.05$). Using the PMR, the ischemic threshold of the extremity is reached at 5 hours.

Conclusions: This study reports a novel and translatable animal model of extremity ischemia and reperfusion correlating ischemic time to functional markers of recovery. In this model an ischemic threshold of 5 hours is defined after which Ligation is associated with less irreversible injury than surgical restoration of flow.

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PS212.

Human Adult Stem Cells Restore Endothelial Migratory Dysfunction in a Hypoxic Environment

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Objectives: Adipose-derived stem cells (ASC) injected into the blood stream following an ischemic event promote therapeutic angiogenesis in affected tissues. It has been suggested that the stem cells exert their influence via a paracrine effect on native endothelial cells (EC). Using an in vitro model, we evaluate the effect of ASC co-culture on EC function in a hypoxic environment.

Methods: Confluent monolayers of human EC grown on the bottom of transwell plates were wounded to create an even 5mm defect and cultured in either normoxic (21%) or hypoxic (1%) conditions. Human ASC were co-cultured on the top of the transwell plates to evaluate a paracrine effect. Subsequently, EC migration was determined by measuring the wound size after 3d. Media samples were collected and VEGF concentration measured via ELISA. To confirm mechanism, ECs were treated with recombinant VEGF at various concentrations and migration measured. HIF-1α expression was evaluated in ASC by Western blot.

Results: Hypoxia inhibited EC migration (0.87 mm vs 0.78mm, $p < 0.05$) over 3d. Co-culture of ASC enhanced EC migration in both normoxic (0.87 mm to 0.93mm) and hypoxic (0.78 mm to 1.02mm; $p < 0.05$) environments. Media from co-cultures in hypoxia contained significantly more VEGF (708.3 pg/mL) than normoxic co-cultures (311.2 pg/mL) and EC alone (28.9 pg/mL). The addition of VEGF to wounded EC cultures improved migration, but not to the extent of ASC co-culture. Finally, hypoxia increased levels of HIF-1α in ASC.

Conclusions: These results demonstrate that: 1) ASC restore and enhance endothelial cell migratory function in a hypoxic environment, and 2) the effect is primarily, but not totally, due to secretion of VEGF by ASC in response to hypoxia. These results suggest that hypoxic pre-conditioning of ASC might be of value in enhancing their role in therapeutic angiogenesis to treat ischemic heart or limb conditions.

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PS214.

Estrogen Stimulates the Cellular Processes of Intimal Hyperplasia Development via ERK1/2 Dependent Signaling Cascades

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Objectives: Intimal hyperplasia (IH) occurs more frequently in postmenopausal women taking hormone replacement therapy. Matrix metalloproteinases (MMPs) play an important role in the cellular processes of IH development. We have previously shown estrogen (Est) increases MMP activity in vascular smooth muscle cells (VSMCs). Est has been shown to activate MAPK signaling cascades, and MAPKs are known to regulate MMPs in various cell types. Here we investigated Est-modulated signaling pathways involved in MMP regulation and their downstream effect on the cellular processes of IH.

Methods: Est receptor antagonist ICI182780 (ICI; 5μM), tamoxifen (Tam; 5μM), or ERK1/2 inhibitor UO126 (UO; 10μM) were added 30min prior to 24h or 5-45min Est exposure (50nM), and cells were subjected to Western blot analyses, and zymography, Boyden chamber migration, and MTT proliferation assays.

Results: Est exposure caused activation of ERK1/2 at 30 min in human female VS MCs, with no activation of JNK, p38, or PI3K at any time point (n = 2-3). Est-stimulated MMP enzymatic activity was inhibited by exposure to ICI and Tam. Est increased VS MC migration by 17 ± 2% and proliferation by 12 ± 2% vs control ($p < 0.05$; n = 8). ICI and Tam inhibited Est-stimulated migration and proliferation to near basal levels. UO inhibited Est-stimulated

MMP-2 activity by $-8 \pm 1\%$ (n = 2), Est-stimulated migration by $-34 \pm 2\%$ ($p < 0.01$; n = 4-8), and Est-stimulated proliferation by $-9 \pm 3\%$ ($p < 0.05$; n = 3), indicating they occur in an ERK1/2 dependent manner.

Conclusions: Estrogen stimulates the cellular processes of IH development via ERK1/2 dependent signaling. Inhibition of ERK1/2 results in downregulation of Est-mediated MMP activity and Est-induced VS MC migration and proliferation. Future studies will include targeted ERK1/2 silencing to assay a possible mechanism for effective IH inhibition. Understanding the signaling mechanisms involved in hormone-mediated IH development could provide a basis for therapeutic strategies of inhibition.

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PS216.

Short-term Diet Induced Obesity Drives Negative Vein Graft Remodeling

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Objectives: Inflammatory pathways are associated with vein graft failure. Short-term high-fat feeding induces a proinflammatory state in perivascular adipocytes, but the longer-term impact of such dietary induced dysfunction on clinically relevant vascular events is unclear. We tested the hypothesis that the inflammatory phenotype resulting from diet induced obesity (DIO) drives accelerated vein graft failure (increased intimal hyperplasia, enhanced negative wall remodeling).

Methods: Male 9-week-old DIO mice (n = 5; 3 wks of high caloric diet) and controls (n = 5) underwent isograft (IVC from same diet donor) unilateral carotid interposition vein graft with a focal mid-graft stenosis. Perfusion fixed vein graft was harvested 4 wks later. DIO/control mice also underwent blood, spleen, and adipose cell harvest for immune profiling (flow cytometry).

Results: Despite a 40% larger body size, DIO mice had 34% smaller residual vein graft lumens ($p = 0.02$). Lumen loss was not due to accelerated intimal hyperplasia, or other differentials in wall thickness (all layer thicknesses and intima/media ratio were equivalent), but rather acceleration of overall negative wall remodeling (cross sectional wall area 47% smaller, $p = 0.03$; outer vein graft perimeter 19% shorter, $p = 0.01$). Resting blood and spleen immune cell profiles were similar; DIO fat held significantly more NK cells, macrophages, and dendritic cells.

Conclusions: These findings highlight negative wall remodeling as a factor leading to vein graft failure, and provide direct evidence that short-term dietary alterations in the mammalian metabolic milieu can have lasting implications relating to acute vascular interventions.

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PS218.

Effect of Remote Ischemic Preconditioning in Liver Ischemia—Reperfusion Injury Produced by Supraceliac Aortic Cross-clamping in a Swine Model of Open Repair of Thoracoabdominal Aortic Aneurysm

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Objectives: Visceral ischemia is inevitable during the open repair of a thoracoabdominal aortic aneurysm (TAAA). Remote ischemic preconditioning (RIPC) has been described as a potential protective measure from ischemia - reperfusion injury (IRI) in various distal tissues. The aim of this experimental study has been to identify any protective effect of RIPC in liver IRI caused during aortic temporal occlusion as performed during a TAAA open repair.

Methods: Three groups of 6 swines each underwent a 30 minutes of aortic supraceliac cross-clamping after a left sided visceral rotation. Liver functional and pathological status was assessed 24 hours after ischemia. The first group was the sham group, the second group was the ischemia - reperfusion (IR) group and the third one was the RIPC group, where remote ischemic preconditioning with a temporary occlusion of the infrarenal aorta was performed before supraceliac aortic cross-clamping. Statistical analysis was done with parametric and non-parametric techniques.

Results: Attenuation of liver damage was noted in the RIPC group as compared to the IR group. Statistically significant reduced values of liver functional markers were found at 24 hours post ischemia between the two groups as follows: alanine aminotransferase (ALT), 36.6 ± 13.5 IU/L in RIPC group vs 58.6 ± 12.5 IU/L in IR group ($p = 0.01$), and aspartate transaminase (AST), 43.4 ± 14.7 IU/L in RIPC group vs 119.5 ± 25.7 IU/L in IR group ($p < 0.001$). With regard to the pathological liver status, the median values of the parameters examined in RIPC and IR groups were respectively: congestion 1 vs 2 ($p = 0.05$), inflammation 1 vs 2 ($p = 0.02$), necrosis 0 vs 2 ($p = 0.02$). No difference was found in liver degeneration (1 vs 1, p = NS).

Conclusions: There is considerable evidence that RIPC with a temporary infrarenal aortic occlusion can reduce the occasionally hazardous liver IRI that is caused during a TAA open repair.